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CERTAIN CLINICAL ASPECTS OF PEPTIC ULCER WITH SPECIAL REFERENCE TO ROENTGEN-RAY DIAGNOSIS AS OBSERVED IN A STUDY OF 743 CASES[1]

By F. H. Baetjer, M. D., and Julius Friedenwald, M. D.,

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In a paper presented at the meeting of the Association of American Physicians in 1912, one of us presented a paper on a clinical study of 1000 cases of ulcer of the stomach and duodenum, and again in 1913 we presented our studies on the value of the X-ray in the diagnosis of this affection. Since then a further series of 743 cases has been studied by us; not only have these cases been followed clinically, but a careful X-ray study was made in every instance. The method followed was identical with that published in our former paper. The cases were first gone into clinically, and then without any note being given as to the nature of the disorder were sent for X-ray examination. The two reports were then placed side by side in order to determine how closely the clinical and X-ray diagnoses corresponded.

Table I.—Illustrating the Incidence of Important Signs and Symptoms in 743 Cases of Peptic Ulcer.

	Cases proven by operation	Undoubted cases of ulcer not confirmed by operation	Somewhat doubtful cases	Total
	185	323	235	743
Definite history of ulceration	163	301	158	622
Pain	169	297	221	681
Tenderness	160	293	188	641
Vomiting	116	208	166	480
Hematemesis	32	67	89	188
Melena	89	155	101	345
Occult blood	103	205	108	421
Normal acidity	54	120	41	215
Hyperchlorhydria	68	95	77	240
Hypochlorhydria	42	62	31	135
Positive X-ray findings	147	272	210	629

[1] Presented at the meeting of the Association of American Physicians, Atlantic City, May 8, 1918.

The 743 cases may be divided into three groups.

Group I.—Cases in which there was an operation, and in which the diagnosis was definitely proven. There were 185 of these cases.

Group II.—Cases which presented such typical clinical symptoms as well as positive X-ray signs of peptic ulcer that the correctness of the diagnosis was positive. These cases numbered 323.

Group III.—Somewhat doubtful cases which presented many of the signs and symptoms of ulcer, but lacked some important signs. In the larger number of these cases the X-ray findings were quite definite. There were 235 of these cases.

Group I.—This group represents the most important in this series of ulcer cases, inasmuch as the diagnosis was definitely confirmed in all instances by operation. It is of interest to note the incidence of the clinical signs in these cases.

Of the 185 patients 132 were males and 53 females. Table II shows the number of cases observed in males and females according to age.

TABLE II

Years	Males	Females	Total
10 to 20	26	4	30
20 to 30	44	11	55
30 to 40	36	32	68
40 to 50	21	3	24
50 to 60	5	3	8

Of the 185 cases a direct history of ulcer was present in 163 (88 per cent); pain in 169 (90 per cent); a tender epigastric area in 160 (86 per cent); vomiting in 116 (63 per cent); hematemesis in 32 (17 per cent); melena in 89 (48 per cent). The stools were examined for occult blood in 128 instances, the findings being positive in 108 (84 per cent).

Of the 185 cases the gastric secretion was examined in 164.

Normal acidity was observed in.....54 cases or in 32 per cent.
Hyperchlorhydria was observed in....68 cases or in 41 per cent.
Hypochlorhydria and anacidity in....42 cases or in 26 per cent.

The percentage of cases of hyperchlorhydria in the series greatly exceeds that in our former series, which is due to the fact that many of these cases were examined by means of the Rehfuss fractional method and thus in many which apparently had presented a normal acidity or subacidity there was in fact hyperacidity.

The X-ray findings in this series of cases are very interesting, inasmuch as the results were definitely checked up by operation.

In the 185 cases of ulcer, the diagnosis as made by the X-ray was verified in 147 (79.4 per cent). Of these 147 cases, in 68 the ulcers were duodenal (46.2 per cent), in 53 gastric (36 per cent), in 17 pyloro-duodenal (11.5 per cent); in the remaining 8 (5.2 per cent) the location of the ulcer was undetermined. In these 8 cases no constant filling defect was obtained, but the functional activity of the stomach was so characteristic that there was no doubt as to the nature of the lesion. Attention will later on be drawn to the importance of this finding, even when no persistent filling defect is revealed.

There remain 38 cases (20 per cent) in this series in which the X-ray findings were either not characteristic or pointed to other conditions.

Of these there was nothing abnormal revealed in 7 instances; in 21 the diagnosis of gall-bladder adhesions was made; in 5, of chronic appendicitis and adhesions in the cecal region, and in 5 the whole picture suggested an enteroptosis. In the 21 cases suggesting gall-bladder adhesions there were filling defects in 8, but these gave the impression of being produced by adhesions and not by ulcer; in 5 instances the diagnosis seemed uncertain, but evidences pointed rather to the gall-bladder, and in the remaining 8 instances the findings were definitely those of a gall-bladder affection.

Group II.—In this group are included those cases which presented such typical clinical signs as well as positive X-ray findings of ulcer that the diagnosis could hardly be questioned. There were 323 cases in this group. Table III shows the number of these cases observed in males and females, according to age.

TABLE III

Years	Males	Females	Total
10 to 20	14	22	36
20 to 30	21	57	78
30 to 40	28	79	107
40 to 50	39	10	49
50 to 60	32	8	40
60 to 70	13	0	13
	147	176	323

In this group of 323 cases there were 301 presenting definite ulcer histories (93 per cent); pain was present in 297 cases (91 per cent); a tender epigastric area in 293 (90 per cent); vomiting in 208 (61 per cent); hematemesis in 67 (20 per cent); melena in 155 (48 per cent). The stools were examined in 255 instances for occult blood, which was found present in 205 (81 per cent).

Of the 323 cases the gastric secretion was examined in 277 instances.

Normal acidity was observed in.....120 cases or 43 per cent.
Hyperchlorhydria was observed in..... 95 cases or 33 per cent.
Hypochlorhydria and anacidity in..... 62 cases or 24 per cent.

X-ray findings in this group were even more definite than in Group I. Of the 323 cases, positive X-ray findings were obtained in 272 (84 per cent).

Of these 272 cases 117 were duodenal ulcers (43 per cent); 109 gastric ulcers (40 per cent); 38 pyloro-duodenal ulcers (14 per cent) and in 8 (3 per cent) the location remained undetermined. A filling defect was absent in the 8 undetermined cases; but here too the functional activity of the stomach was so definite that a positive diagnosis of ulcer was made with almost absolute certainty.

There were 51 cases (15.6 per cent) in this group in which the X-ray findings were either uncertain or pointed to some other pathological conditions.

Of these cases no abnormality was discovered in 12 instances; in 29 the diagnosis of gall-bladder adhesions or of a chronic appendicitis was made. In the 29 cases a filling defect was observed in 11, which was regarded as due to adhesions and not to ulceration; notwithstanding these X-ray findings the clinical signs were so definite that the diagnosis of ulcer appeared justifiable.

Group III.—We have put in this group those cases that presented many of the manifestations of ulceration, but in which there still appeared some element of doubt as to diagnosis. In some of these cases there were few clinical signs except hemorrhage, while the X-ray pointed to ulcer; in other cases the clinical signs indicated ulceration, while the X-ray either revealed no lesion in the stomach whatever or else pointed to some affection in a more distant portion of the abdominal cavity. In no inconsiderable number of cases the history of ulceration was so definite that the diagnosis appeared unmistakable; yet the gastric secretion presented an absence of free hydrochloric acid, there was no history of hemorrhage, nor was occult blood found in the stools at repeated examinations.

The diagnosis was definitely cleared up in many of these instances by positive X-ray findings.

Table IV presents the cases of ulceration observed in this group, in males and females, arranged according to age. Of the 235 patients 121 were males and 114 females.

TABLE IV

Years	Males	Females	Total
10 to 20	4	6	10
20 to 30	15	8	23
30 to 40	29	49	78
40 to 50	37	28	65
50 to 60	32	15	47
60 to 70	4	8	12

In this group of 235 cases there were 158 presenting a definite ulcer history (67 per cent); pain was present in 221 cases (94 per cent); a tender epigastric area in 188 (80 per cent); vomiting in 156 cases (66 per cent); hematemesis in 89 (37 per cent); melena in 96 (40 per cent). The stools were examined in 133 instances for occult blood, which was found present in 108 (81 per cent).

Of the 235 cases the gastric secretion was examined in 149.

Normal acidity was observed in.....41 cases or 27 per cent.
Hyperchlorhydria was observed in .....77 cases or 51 per cent.
Hypochlorhydria or anacidity in.....31 cases or 22 per cent.

In this group of 235 cases the X-ray findings were so outspoken in 210 instances (89.7 per cent) that, notwithstanding the absence of certain of the clinical signs, the diagnosis of ulcer seemed justified. Of the 210 cases in 80 (38 per cent) there were duodenal ulcers; in 88 (42 per cent) gastric ulcers; in 25 (11 per cent) pyloro-duodenal ulcers, and in 17 (8 per cent) the location of the lesion remained undetermined. In these 17 cases a filling defect was not observed, yet here too the functional activity of the stomach was so characteristic that there remained but little doubt as to the diagnosis. There remain 25 cases in this series (12 per cent) in which the X-ray findings were not characteristic of ulcer or else pointed to other conditions. Of these nothing abnormal was observed in 8 instances in the plates; in 9 gall-bladder adhesions were shown, and in 8 chronic inflammatory changes in the right lower quadrant indicating the presence of a chronic appendicitis.

The X-ray findings in uncomplicated cases of gastric and duodenal ulcer are, as a rule, very definite as well as constant. The signs ordinarily observed are not unlike those described by us in a former communication.

It is only within the last years that we are beginning to observe results upon which reliance may be placed. The old theory that it was possible to diagnose ulcer from the adherence of bismuth to the raw surfaces has now been practically abandoned, inasmuch as experience has taught us that this rarely happens because the irritability of the raw surface produces hypermotility with violent contractions, which render it almost impossible for the bismuth to adhere to the raw surfaces. At present we lay stress on the way the stomach and intestines function as well as upon the actual demonstration of the ulcer. Curiously enough, the diagnosis of duodenal ulcer is much simpler than that of gastric ulcer.

We can practically always rule out the presence of a simple duodenal ulcer, but we cannot always rule out gastric ulcer. The main distinction lies in the fact that in an irritating lesion of the stomach, such as ulcer, the consequent hypermotility causes a tonic contraction of the pylorus with retention of the gastric contents over a shorter or longer period, as well as a deformity, according to the situation of the ulcer. On the other hand, in lesions of the duodenum, we have indeed a hypermotility not only of the duodenum, but of the stomach itself; but in this case we do not have the spastic condition of the pylorus, consequently the hypermotility produces a rapid emptying of the stomach contents. For example, in our experience, in simple ulcer of the duodenum not complicated by adhesions, we find that the stomach will invariably extrude the greater part of its contents in from fifteen or twenty minutes to an hour. There are in addition certain characteristic features connected with this lesion; we have a decided hypermotility, but the contractions are quite uniform, and there is no tendency toward hour-glass formation of the stomach. The pylorus is patulous and the bismuth flows quite freely into the duodenum. The duodenum is in very active contraction, and in many cases we find that there is a deformity in some portion of it, and this defect persists throughout the period of the examination. At times we may observe bismuth running along either side with the defect between the two bismuth currents.

In gastric ulcer we have just the reverse. There will be primary quick expulsion of contents and then the spastic condition of the pylorus appears with hour-glass formation, and we have a retention, lasting anywhere from four to six hours, according as the lesion is simple or is complicated by adhesions. In addition a filling defect is usually observed which remains constant in all examinations.

The differentiation between gastric and duodenal ulcer from clinical signs alone is often very difficult, and not a few clinicians hold that in many instances it is impossible. The X-ray findings in the two conditions, however, differ so markedly that in them we possess an almost positive means of differentiation.

In our combined series of cases positive X-ray findings were noted in 84.4 per cent of all cases examined. Of these 42 per cent represented duodenal ulcers; 39 per cent gastric ulcers; 12 per cent pyloro-duodenal ulcers; in 8 per cent the location of the lesion was undetermined.

While the functional activity of the stomach from a roentgenological point of view may indicate the presence of an ulcer, the filling defect or deformity may be absent and may not be revealed in the plates, owing to the fact that only when the lesion is situated on the anterior surface of the stomach and along the anterior surface of the lesser and greater curvatures can this condition be observed. According to our observations the functional signs are often as important as the presence of the defect in arriving at definite conclusions. This condition is especially well illustrated in the healing of ulcers (attention to which will be called later on) in which, although the defect may still remain in the form of a cicatrix, the functional activity of the stomach may have become entirely normal.

In 8 per cent of our cases there were no defects observed, yet the functional activity of the stomach pointed definitely to ulcer.

The greatest difficulties arise in the diagnosis of complicated cases; that is, when adhesions are present, due either to the healing of the ulcer or to inflammations connected with one or other of the organs in the abdominal cavity. These adhesions so frequently mask the usual findings, that it is often impossible to determine whether we are really dealing with an ulcer or whether a lesion of some other organ is causing the symptoms. Such adhesions may arise from the ulcer itself, from the gall-bladder or appendix, or there may be no adhesions at all in the region of the stomach, and the gastric findings may be due to a purely reflex condition or to spasm.

It is necessary at times, in a certain proportion of cases in which adhesions of the stomach are present, to lay especial stress upon the clinical history of the case before a final decision can be made. If the clinical signs coincide with a definite history of ulcer, we must conclude that the adhesions have taken their origin from the ulcer; if of cholelithiasis, from the gall-bladder; and so on, inasmuch as from a roentgenological point of view the appearances are frequently identical.

In 9 per cent of the cases in our series the diagnosis was rendered doubtful by the presence of adhesions.

As has been pointed out, unless due care be exercised, one may easily be misled by certain reflex or spastic conditions of the stomach. It is not uncommon to observe a stomach presenting a persistent filling defect in a definite area and continuing over a period of an hour or two—in a single instance under our observation it persisted for 48 hours. In doubtful cases, spasm of the stomach can easily be eliminated by the administration of full doses of atropin for one or two days, until the patient is well under its influence. A second examination, made under these conditions, will immediately show that the suspicious area has completely vanished, and that the condition previously observed was due to spasm.

Additional evidence of the presence of an ulcer when situated at or near the pylorus is the presence of obstructive signs produced by the cicatrix while the ulcer is healing.

Clinically, the diagnosis of *gastrectasia due to stenosis of the pylorus* is usually not difficult, especially when the cardinal symptoms of this disease are present. The vomiting of the collective type, together with peristaltic or antiperistaltic waves, suggest the diagnosis; and this becomes even more certain when remnants of food are obtained from the fasting stomach in the morning, and especially when the gastric contents are of the three-layered variety, and contain numerous sarcinæ; or when the rice test of Hausmann or the chlorophyle test of Boas is positive. But we all know that these findings are present only when the obstruction is marked or nearly complete, and that there is a large number of cases in which obstruction is suspected, and yet many weeks often elapse before the stenosis becomes sufficiently marked to warrant a positive diagnosis, for the symptoms already noted occur only as late manifestations of the disease, and are not present or are observed only occasionally as early signs. At times spastic contractions of the pylorus due to former ulcers or the irritation exerted by the gastric contents upon erosions and fissures in this region afford similar signs.

In this condition, when the X-ray examination is made, a typical sack-like formation is observed, and all the bismuth rests at the bottom of the fundus. Under such conditions the examination will show a retention of contents for from 10 to 20 hours.

In the early stages of gastrectasia, that is, when the obstruction is still incomplete, the diagnosis is often very difficult. The condition is due to a partial stenosis of the pylorus, and inasmuch as the symptoms produced by it are quite vague, the condition is often overlooked, or an incorrect diagnosis is made.

The physical signs of the disease are not marked, peristalsis being usually absent and vomiting occurring irregularly, the vomitus being devoid of the usual features occurring in gastric stasis. A symptom very frequently present is pain, appearing some time after meals and becoming most intense 2 or 3 hours after the ingestion of food.

This pain is due to the pyloric spasm produced by the incomplete obstruction, and is temporarily relieved by the ingestion of food or of alkalies. As is well known, this symptom is characteristic of ulcerative lesions in the pyloric or juxtapyloric region, but since in many instances partial obstructions have their origin in pyloric and juxta-pyloric ulcerations, this symptom is valuable as an early sign of the disease. As additional evidence of the presence of partial stenosis is the existence of gastric secretion in the fasting stomach, especially if it is observed in frequent examinations. If the fasting stomach is constantly empty of gastric secretion, partial stenosis may usually be excluded. The diagnosis may be based, therefore, on the presence of secretion in the fasting stomach, occurring continuously or intermittently, together with stasis, even of a small amount, appearing at more or less frequent intervals.

These signs appear, however, so intermittently that they are often overlooked, especially when overshadowed by the usual symptoms of dyspepsia occurring in this affection. The X-ray has given us a means of more thoroughly solving this difficult problem.

In the early stages of this condition we have active contractions with the slow extrusion of the stomach contents. Now a normal stomach extrusion gets rid of its bismuth meal in from three to six hours. Generally, we observe that the high stomach occupying the horizontal position empties itself much more quickly than the prolapsed fish-hook variety, so that it might be stated that from 3 to 4 hours is the normal rate of emptying for the horizontal stomach, and from 5 to 6 hours for the prolapsed fish-hook variety. When in these various types we note that, while the contractions are good but the expulsion of contents is slower than under normal conditions, we must consider the possibility of some beginning obstruction.

A second very significant sign is the fact that in the study of the plates we frequently observe that a portion of the stomach just within the pylorus on the greater curvature in the prepy-

loric region shows a tendency to bulge. This condition is produced by the active contraction of the stomach, forcing all of the food towards the pyloric region. The pylorus not being patent, the prepyloric portion of the stomach becomes dilated under this constant pressure, so that the plate presents the pylorus not at the end of the stomach, as it were, but with the prepyloric region extending further to the right than the pylorus, the pylorus resting on the top of the stomach, and pointing to the splenic region. The prepyloric bulging is dependent largely upon the duration of the affection. In early cases it is very slight, but as the condition advances the prepyloric bulging may reach the size of a hen's egg. If the condition persists, dilation begins to take place, and after a time practically the entire fundus yields, so that a typical sack-like formation is produced, and all the bismuth rests at the bottom of the fundus.

In 20 per cent of our cases there were evidences of obstruction with dilatation of the stomach, in 12 per cent of these partial obstruction was observed.

In a certain number of cases there are definite clinical evidences of ulceration, and yet the X-ray presents no indication whatsoever of this condition. This may be due, as we have already pointed out, in some instances, to adhesions masking the true condition, but the absence of definite X-ray signs cannot always be traced to this factor. It happens at times that a complicating chronic appendicitis or cholecystitis may be so marked as to mask any findings in the stomach itself, and the significance of a small filling defect might easily be overlooked.

In one of our cases (Dr. B.), a man of 64 years of age, who had presented definite clinical signs of duodenal ulceration for years, and in whom the X-ray findings had been positive 4 years previously, our examination gave evidence of gall-bladder adhesions and no signs of ulceration. At operation a large duodenal ulcer with adhesions was found. In another instance (Mrs. B.), the X-ray findings pointed to a chronic appendicitis, whereas the clinical evidences were definitely in favor of ulcer. At operation a definite indurated duodenal ulcer was found.

In our entire series there were 3 per cent of cases of ulceration in which the X-ray signs gave no evidences of the actual condition, and in 15 per cent they were indefinite.

Although ulcerations are not always revealed by X-ray examinations, there are many cases of ulcer doubtful from a clinical standpoint in which the ray will clear up the diagnosis. In two of our cases the clinical signs were indefinite, but suggested an appendicitis; the X-ray was definite as to ulcer in both instances. Appendectomy was performed, and only temporary relief was afforded; there was subsequent gastric hemorrhage and finally operation revealed an ulcer in each instance. Another patient (Mr. McE.), a man aged 66, gave a history of very indefinite gastro-intestinal symptoms. The X-ray revealed ulceration; a sudden large gastric hemorrhage showed the correctness of this finding. The X-ray is, therefore, of the greatest help in pointing to the current diagnosis in doubtful cases. In 1 per cent of such indefinite cases in our entire series the X-ray cleared up the diagnosis.

There are cases, however, in our experience in which the diagnosis of either chronic appendicitis or cholelithiasis is made not only from a clinical, but also from a roentgenological standpoint, but which at operation present no evidence of such conditions, ulceration of the stomach or duodenum being found, although the X-ray plates have shown no evidences pointing to either affection. Finally, there still remains another group of cases in which the ulcerations are of the so-called mucous type. These are easily demonstrated by means of the X-ray, but are rarely observed at operation unless the stomach itself be incised. It frequently happens that such cases come to operation, and yet no abnormality is observed at the exploration. This is due to the fact that while both mucous and penetrating ulcers are alike easily discernible by means of the X-ray, we have as yet no means of distinguishing between such conditions, except in those instances in which large indurated or perforating ulcers are present.

In the X-ray study of *gastric ulcer* the differential diagnosis between this condition and *gastric carcinoma* is often very difficult. It is still a much debated question whether carcinoma of the stomach has its origin primarily as such, or is the result of a transition from an ulcer. If the latter view be correct, one can readily understand the difficulty in determining when the benign condition enters the stage of transition into malignancy. The situation of both ulcer and carcinoma is very frequently the same, although we observe ulcer more frequently than carcinoma on the lesser curvature.

In the differential diagnosis between the two conditions the points to be taken into consideration are as follows:

1. *Peristalsis.*—In ulcer there is always hypermotility with a spasm of the pylorus and more or less retention of contents. In carcinoma, unless there is obstruction, there is always hypermotility with rapid evacuation of contents.

2. *Position.*—Ulcer is generally observed on the lesser curvature near the pylorus, although it may occur on the greater curvature and is frequently found in the duodenum. Carcinoma may occur in any part of the stomach. The invasive lesions are more frequently seen on the lesser curvature near the pylorus, and less frequently on the greater curvature. The massive growths are more generally seen on the greater curvature.

Filling Defect.—In ulcer the filling defect is much smaller and is not apt to have the immediate peristaltic waves interfered with, although, if the inflammatory area be large, there may be a dead area surrounding the filling defect. In carcinoma the filling defect is generally surrounded by an invasive area, which, although not appearing on the plate, interferes with motility, producing an apparently large dead area. In ulcer of the pylorus there is a filling defect, but it does not generally assume a crater-like appearance. Carcinoma of the pylorus in the earliest stage is generally annular and produces a crater-like appearance.

When any of these conditions pass on to the obstructive stage, the change that is caused by the dilatation may mask the signs associated with the filling defect.

In our experience, in the very early stages of gastric cancer, it is frequently impossible to determine whether we are dealing with a malignant or a simple ulceration. Our main aim, however, is to decide whether the lesion at hand is really an ulcer or not. Inasmuch as indurated gastric ulcers have at times a tendency to become malignant and produce roentgenograms similar to those which are cancerous, they must be included in the same class. The exact diagnosis must be cleared up by further investigation into the clinical history and by the examination.

But even under these conditions there are many cases in which the diagnosis may still remain in doubt until operation, and, in some, microscopic examination of the specimen after removal may be necessary in order to establish the true nature of the disease.

In our series there were 1.1 per cent of cases in which the ulcer was mistaken for carcinoma; in a larger percentage, however, carcinoma was mistaken for ulcer.

Now that we have taken up the positive phase of the diagnosis of ulcer, it is wise to draw some conclusions as to the *negative findings*. In the first place we believe that we can rule out positively the presence of a duodenal ulcer. If we observe that the stomach contents are not expelled promptly, and that the greater portion remains after the lapse of an hour, we can maintain confidently that the trouble is not in the duodenum. Even in the old chronic ulcer, with adhesions, the motility is so marked that it cannot be overlooked. The negative diagnosis of gastric ulcer is also of importance. However, so many complicating phases are present in these cases that the retention of bismuth in the stomach does not appear to have quite the same significance as the hypermotility in duodenal ulcer. The absence of a filling defect in the stomach or of a deformity of the duodenal cap is a significant sign pointing against ulcer.

As has been shown, in gastric ulcer, we have a spastic retention. In simple atony and in prolapse we may have retention and yet the spastic character of the retention is not present, nor is there any tendency toward the formation of an hour-glass stomach.

The absence of any of the positive signs of ulcer by means of the X-ray examination has been of the greatest help to us in excluding the presence of ulcer. This method has been especially helpful in the diagnosis of atypical conditions and affords us the most positive method of excluding ulcer.

There have been 698 cases in which we have been able to exclude the presence of ulcer by this method of examination.

Another very important point which our X-ray studies have brought out in connection with ulcer is that the degree of healing can be determined by this method. We were among the first to call attention to the fact, and other clinicians have since corroborated this finding. In ulcer, when the patient is given a rest-cure treatment, all symptoms gradually disappear and the patient becomes, comparatively speaking, well. This usually takes place in from 4 to 5 weeks. At the end of this time, however, if a second bismuth examination is made, we often find the same characteristic signs as in the first ulcer, though the patient shows no symptoms whatever. In a series of ulcer cases, that have been examined in from 3 to 4 weeks after an absence of symptoms, we have frequently found but little change in the defect or motility of the stomach.

When these patients are given the ordinary diet these symptoms may recur in a short time. If treatment is continued, however, our experience has demonstrated that, as the ulcer continues to heal, the motility of the stomach returns to a more normal condition, and by making repeated X-ray observations over a long period of time we can observe when the ulcer has healed.

There can be no question that this is one of the most important findings of this work, inasmuch as, until this method was employed, there was absolutely no means of determining whether an ulcer had healed or not. Our only means of determining this question has been a return of symptoms when the patient was placed upon an ordinary diet, and this simply meant a relapse for the patient. By means of the X-ray examination made from time to time we are enabled to determine the progress of healing. This method has been utilized to great advantage by us in 321 of our cases (43 per cent).

There is another fact of great importance connected with the healing of ulcers brought out by this method of examination. We observed that not infrequently, after an ulcer has completely healed, another ulcer may take its origin, sooner or later, either at the same location or at another, either in the stomach or duodenum. This finding was demonstrated by us in 64 instances (8 per cent). In the largest number of these cases there can be but little question but that the ulcer must have been caused by some focal infection for, curiously, in some instances after the removal of the infection there was no further recurrence.

Finally, important evidence is further obtained by means of the X-ray as to the extent of the ulcer and degree of induration, as well as the degree of obstruction, and thus we are guided in determining in a measure whether surgical interference should or should not be undertaken. Of the 185 of our cases which were operated on, the X-ray demonstrated the necessity of the operation in 147 cases (79.4 per cent).

Conclusions.—From our studies on the many cases of peptic ulcer in which X-ray examinations were made, we believe that we are justified in drawing the following conclusions:

1. The X-ray offers most valuable assistance to the diagnosis of peptic ulcer, and although this method is not yet sufficiently well developed to be relied upon alone without entering into the clinical aspects of the disease, it is of the greatest diagnostic help in obscure cases.

Positive X-ray findings are noted in about 84 per cent of cases of peptic ulcers and in 79 per cent of cases operated upon.

2. In duodenal ulcer there is excessive hypermotility of the stomach with rapid evacuation of the contents, so that the greater portion is extruded within the first half hour; there is hypermotility of the duodenum with formation, usually, of a deformity which remains fixed in all of the examinations.

3. The diagnosis of gastric ulcer is dependent upon two conditions, namely, the functioning of the stomach, and the

finding of the filling defect. It is only when the filling defect is situated along the anterior surface of the stomach and along the anterior surface of the lesser and greater curvatures that it can be demonstrated. On the other hand, it matters not what the situation of the ulcer is, the functions of the stomach are materially affected. We have in this condition an excessive irritation from the ulcer, with consequent hypermotility and a spastic condition of the pylorus, so that for the time being there is practically no expulsion of bismuth. It is only when the spasticity relaxes that a portion of the bismuth is expelled. In gastric ulcer, wherever its situation, we can always look for a certain amount of retention of contents. There is always a more or less marked hour-glass formation. According to our observations the functional signs are often as important as the presence of the filling defect in arriving at definite conclusions, inasmuch as in 8 per cent of our cases, although there were no defects found, the functional changes pointed definitely to ulcer.

4. The greatest difficulties arise in the diagnosis of complicated cases; that is, when adhesions are present. These so frequently mask the usual findings that it is often impossible to determine whether there is really an ulcer of the stomach at hand or a lesion of some other organ. When the ulcer is situated at or near the pylorus, signs of partial obstruction frequently aid in establishing the diagnosis.

5. The X-ray affords an almost absolute means of differentiating between gastric and duodenal ulcer.

6. By means of the X-ray examination we can generally rule out the presence of ulcer.

7. We can approximately determine the degree of healing as well as recurrence of an ulcer which cannot be as certainly determined in any other way.

8. One can obtain sufficient evidence as to the extent and induration of the ulcer and degree of obstruction to guide us, in a measure, as to the necessity of surgical intervention.

EXPERIMENTAL MENINGOCOCCUS MENINGITIS

By CHARLES R. AUSTRIAN, M. D.

(From the Medical Clinic, The Johns Hopkins Hospital)

In 1915 Black[1] published observations concerning the use of prophylactic vaccine to prevent the development of epidemic cerebrospinal meningitis. Shortly thereafter this study was undertaken experimentally to test the efficacy of the procedure.

Owing to the proximity of the laboratory to the wards of the hospital, and because of limited funds, monkeys were not to be had for the experiments, and the attempt to utilize a smaller animal was made. The rabbit was chosen, and a satisfactory technique for the production of meningeal infection was elaborated, the details of which have been published in a previous communication.[2] In brief, it was found that a needle can be readily introduced into the spinal canal of a rabbit, that material can be injected through it into the lumbar (or other region) of the canal, and that substances thus injected are rapidly spread throughout the subdural space. Spinal puncture was always carried out only after the animal had received a light ether narcosis.

The disadvantages inherent in the use of rabbits in the study of meningeal disease are two: First, it is difficult to avoid injury to the spinal cord when injections are made; secondly, the spinal fluid, normally and in disease, is so scanty that withdrawal of it by aspiration is impossible and one is thus deprived of the means of *intra-vitam* determination of the presence or progress of infection.

The method perfected, suspensions of meningococci were introduced into the spinal canal of rabbits of approximately the same size and weight and that were kept under identical conditions. It was found that white rabbits were more desirable than other varieties.

Some of the strains of meningococci were obtained from the Rockefeller Institute through the courtesy of Dr. Louise Pearce; others were isolated from the spinal fluid of patients with epidemic cerebrospinal meningitis. The variable virulence of the organisms necessitated the use of a number of strains before a suitable one was obtained. The particular one used in most of the following experiments was a relatively attenuated one recovered from a case of subacute meningitis (Thomson) admitted to the medical service of The Johns Hopkins Hospital.

This strain, like others employed, was identified as a pure meningococcus by morphological and staining characteristics, cultural and fermentation tests, and by agglutination with anti-meningococcus serum. The cocci were planted on blood- or serum-agar slants and incubated for 20 hours at 37° C. A homogeneous suspension of the growth on the surface of two such slants was made in sterile 0.85 per cent salt solution and 0.5 to 1.5 c. c. were used for the injections. All suspensions were injected within 45 minutes of preparation.

Some of the animals that received injections died within 12 to 24 hours, and at autopsy showed no gross lesion except hyperæmia of the meningeal vessels. The larger number developed a typical clinical picture of meningitis and showed characteristic anatomical changes. The following two protocols are illustrative:

January 12, 1915. Rabbit 317. White, female, weight 2000 grams. The lower back was clipped, shaved and cleaned with tincture of iodine. The animal was then etherized and a needle was introduced between the two upper lumbar vertebræ. Recovery from narcosis was complete in 10 minutes and 1.5 c. c. of a suspension of meningococci prepared as described were slowly injected. Following a period of restlessness, paresis of the hind quarters and helpless inertia of 30 minutes' duration, the animal

[1] Black, J. L.: Jour. A. M. A., 1914, LXVIII, 2126.

[2] Austrian, C. R.: BULL. JOHNS HOPKINS HOSPITAL, 1916, XXVII, 237.

recovered except for weakness of the left hind leg. Sixteen hours later, the rabbit was found lying on its right side with spastic hind quarters, extended forelegs, clonic jerking of the head and irregular respiration. Two hours later, there were retraction of the head, rigidity of the cervical muscles and clonic convulsions. Twenty-four hours after injection the animal was found dead.

Autopsy.—Well-nourished rabbit in position of opisthotonus. Except for the lesions in the nervous system the viscera appeared normal. The spinal meninges were moderately injected, a small amount of turbid fluid had accumulated over the thoracic cord, and over the dorsum of the medulla, pons and cerebellum there was a very turbid, gelatinous exudate. Over the convexity of the brain there was an unusual grade of congestion of the dura and pia, and the same condition was noted over the base of the brain with a small amount of gelatinous exudate. There was no marked reaction along the olfactory bulbs. Fresh smear preparations from the dorsum of the pons showed very many polymorphonuclear leucocytes and a few red corpuscles. Stained smears showed clumps of pus cells and myriads of gram-negative diplococci, a number of them intracellular. Cultures from the exudate showed typical meningococci. Smear preparations and cultures from the nose failed to show the organism.

January 12, 1915. Rabbit 318. White, female, weight 2100 grams. This animal was prepared in the same way as Rabbit 317 and received an intraspinous injection of 1 c. c. of the same suspension of organisms. The injection was followed by coma of 25 minutes' duration, after which the animal was ataxic for a short time. Four hours after injection the animal was dull, its head was strongly retracted, respiration irregular, and there were jerkings of the hind legs. Seventeen hours after injection the rabbit was found dead in its cage.

Autopsy.—Well-nourished rabbit with head sharply retracted. Large blood clots in the nose. Except for the lesions in the nervous system the viscera appeared normal. The striking finding in the central nervous system was the extreme congestion of the meninges. The hyperæmia extended into the sulci of the brain and was more marked over the base than over the convexity. There was a small excess of cloudy fluid over the dorsal aspect of the brain-stem and many minute hæmorrhages beneath the pia. The olfactory bulbs showed nothing striking, but the nasal mucosa was very much injected and showed a number of small hæmorrhages. Smear preparations from the exudate at the base of the brain and over the pons showed numerous polymorphonuclear leucocytes and gram-negative diplococci, mainly extracellular and in various stages of degeneration. Meningococci did not grow in cultures from nose or spinal exudate.

In six of the ten animals included in this series, the meningitis that developed ran a rapidly lethal course in from 20 to 36 hours. In three, after a period of symptoms varying from one to five hours, recovery followed. It was not possible to produce a chronic form of the disease in untreated animals.

It is worthy of note that smears and cultures from the nasal mucous membrane of Rabbit 317 showed the presence of meningococci, for this observation definitely establishes the finding of Flexner that this organism may be excreted through the nose.

The reaction to infection in the rabbit differs from that seen in man and in monkeys in the small amount of fibrin in the exudate and the scanty increase of cerebrospinal fluid. In only two of the ten animals included in this group did a blood invasion occur. It was apparent that cocci introduced into the spinal canal in the lumbo-sacral region soon became distributed along the meninges and gave rise to an inflammatory reaction most marked at the base of the brain. This finding corresponds to that of Flexner in the experimental meningitis of monkeys, and, as he has indicated, is evidence that speaks against a basal localization as indicative of infection from the nose.

At this juncture we departed from our original purpose and attempted to find out whether or not a meningococcal meningitis could be produced by routes of infection other than the intraspinal one.

The idea generally accepted since the time of Weigert of the direct invasion of the meninges by the passage of meningococci from the nasal mucosa through the ethmoid sinus to the base of the brain seemed to us, as it had to others, open to question. The occasionally demonstrated occurrence of a bacteriæmia in the course of the disease in man might indicate as well the septic nature of the disease with a metastatic localization in the meninges as an overflow into the blood stream from a primary meningeal focus. The latter view seems more probable when it is recalled that the blood culture is more likely to yield positive findings early in the course of the illness. Moreover, it seems illogical that the direct route should be the path of election, as the mucous membrane of the nose and the meninges themselves, unless already diseased, should act, in a measure at least, as a protective barrier.

With these ideas in mind, the following experiments were made:

Series A.—Each of 20 rabbits was given an injection of varying amounts of the standard suspension of meningococci (Thomson) into the nasal mucous membrane. At different intervals after treatment the animals were killed by a blow on the head and cultures and smears of the heart's blood and meninges were studied.

Not one of these animals developed meningitis. In not one could the organism be demonstrated in smear or culture from the cerebral or spinal meninges. Two of the rabbits developed positive blood cultures, but the blood invasion may have been due to a direct injection into a small blood vessel of the nose.

Similar results were obtained when a fresh ointment of meningococci in vaseline was roughly rubbed into the mucous membrane of the nose.

Series B.—Each of a group of 15 rabbits was given an injection of the standard suspension into an ear vein, and at intervals varying from 10 to 50 minutes after inoculations cultures were made of the blood and from the meningeal surfaces.

The micrococci disappeared from the peripheral circulation of these animals in from 15 to 75 minutes. None of this group developed meningitis and none showed the organisms in smears or cultures from the meninges.

The inability to infect the normal cerebrospinal canal of rabbits either by the intranasal or the intravenous injection of the meningococcus was definite.

Mindful of the recognized fact that the interchange between the meningeal and systemic circulations is enhanced by hyperæmia of the choroid plexus and of the meningeal vessels, the effect of preliminary irritation of the meninges and subsequent

possible infection through the nasal cavity or through the general circulation was studied.

Rabbits that received a subdural injection of fresh or of inactivated rabbit serum did not develop any symptoms except those due to temporarily increased intracranial pressure (dyspnœa, twitching or coma of short duration), symptoms identical with those following the introduction of an equal quantity of salt solution. When killed and examined within 30 to 60 minutes after injection, marked engorgement of the meningeal vessels was found.

Series C.—Fifteen normal rabbits were each given an intraspinous injection of 0.5 c. c. of normal rabbit serum. Thirty to sixty minutes after this preliminary treatment each received 1 c. c. of the standard suspension of meningococci by direct injection or by rough inunction into the mucous membrane of the nose. In none were the organisms demonstrable in smears or in cultures made from the surface of the meninges, 5, 10, 15 or 24 hours after the organisms had been introduced.

Series D.—Each of 20 rabbits received a preliminary intraspinous injection of 0.5 to 1.0 c. c. of normal rabbit serum and 30 to 50 minutes later was given an injection of the standard suspension of meningococci into an ear vein. The exact technique of this procedure and the results of this experiment are shown in the appended protocol:

March 12, 1915. Rabbit 345. White, male, weight 1800 grams. The lower back was clipped and cleaned with tincture of iodine and the animal was given a light ether anæsthesia. A needle was inserted into the spinal canal in the lumbar region and 2.0 c. c. of normal rabbit serum were injected. Injury of the cord caused twitching of the tail and spastic palsy of the left hind leg, and dyspnœa, coma and ataxia developed. Thirty minutes later 2.0 c. c. of the standard suspension of meningococci were injected into the ear vein. Three hours after the intravenous injection the animal was dull, inert, but markedly hyperæsthetic to sound and touch. Twenty hours after injection the animal was very excitable when aroused, inert when undisturbed. There was no muscle rigidity, no retraction of the head. Eight hours after this observation the animal was killed.

Autopsy.—**Well-nourished rabbit. General examination was quite negative. The meninges over the spinal cord showed nothing strikingly abnormal. There was a punctate hæmorrhage where the needle had penetrated the cord. Over the dorsal surface of the pons there was a marked excess of turbid fluid containing fine flecks of fibrin. The vessels of the pia and dura were markedly congested, and over the base of the brain there was a definite excess of sero-fibrinous exudate. Stained smears from the exudate showed polymorphonuclear leucocytes and many gram-negative diplococci, mainly extracellular. Cultures from the surface of the pons and the base of the brain gave a pure culture of typical meningococci. Cultures from the heart's blood and spinal meninges were sterile.**

In 20 experiments of this type, eight of the animals died within 8 to 12 hours after injection without clinical evidence of meningeal irritation and at autopsy no meningitis was found. From the meninges of two animals killed one hour after intravenous injection, the meningococcus was identified in smears, and from the spinal canal of one of them the organism was obtained in culture. Three others of this series developed a typical fatal meningitis. The remaining seven animals after symptoms lasting 30 minutes to two hours recovered completely. It is unfortunate that some of these were not sacrificed at short intervals to determine if the cocci had penetrated the central nervous system.

This experiment demonstrated that meningococcal sepsis in the rabbit may lead to the development of a metastatic meningitis when there is a pre-existent hyperæmia of the meninges. The development of an outspoken inflammation of the cerebral and spinal membranes was inconstant, but the clinical and anatomical findings were characteristic.

The results of the foregoing studies seemed clearly to justify the following conclusions:

(1) The cerebrospinal canal can be infected by way of the blood stream.

(2) Though under normal conditions the presence of a bacteriæmia does not lead to the development of meningitis, when a condition of hyperæmia of the thecal vessels exists, meningeal inflammation may result.

(3) Neither when normal conditions are present nor when meningeal irritation has been induced do meningococci introduced into the nasal mucous membrane gain access to the meninges.

(4) The demonstration of meningococci in the nasal secretion is to be interpreted as evidence of the excretion of these organisms by this route, but the conclusion is not necessarily warranted that they find a direct portal of entry to the meninges by the same channel.

These observations seem important from an etiological standpoint. They indicate the probability that epidemic cerebrospinal meningitis, as it occurs in man, is to be regarded as a metastatic disease developing in the course of a general infection, rather than as the evidence of a primary local disease. They do not necessarily indicate the portal of entry of the invader, nor antagonize the view that the cocci are taken into the body through the upper respiratory tract, a fact apparently established.

The observation that meningococcal sepsis in rabbits is followed by the development of meningeal disease only when the meninges are not in a normal state is suggestive and may explain in part, at least, the occurrence of the disease in some of those exposed and its failure to develop in others in like contact with sources of infection.

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JOHN R. YOUNG, PIONEER AMERICAN PHYSIOLOGIST[1]

By Howard A. Kelly, M. D.

John R. Young, a student at the University of Pennsylvania, submitted, in 1803, for the degree of doctor of medicine, a remarkable thesis entitled, "An Experimental Inquiry into the Principles of Nutrition and the Digestive Process." Allow me to premise my subject with a brief general review of the history of digestion in order that we may do full justice to his claims as we recognize the conditions under which he labored and the obstacles he had to overcome.

In the effort to clarify the mystery enveloping the processes of digestion, many bizarre views have been current from the days of the ancients down to recent times.

An *animistic* doctrine held that an archæus, a mysterious spirit resident in the living organism, was the potent factor in the appropriation of the nutriment from the ingested substances, which being interpreted means, I suppose, that it is a vital process, as inexplicable as life itself.

Another view was that *trituration* and *attrition*, so easily observed in the stomachs of grain-eating birds, did the work. This mechanistic notion, coming down from the days of Erasistratus of Alexandria, met its downfall in a *reductio ad absurdum*, at the hands of Archibald Pitcairn (1652-1713), a Scotch physician and poet, and one of the original members of the Royal College of Physicians of Edinburgh, incorporated in 1681. Naïvely taking Borelli's estimate of the power developed by the flexor muscles of the thumb, and weighing these, and then weighing the stomach with all the surrounding abdominal muscles and comparing them, he easily reached the astonishing calculation that the available compressing and crushing force of the stomach was over four hundred thousand pounds!

Putrefaction was a notion which also held sway for ages. Later, when it had been recognized that putrefaction was a form of fermentation, associated with certain well-defined and observable phenomena, this view seemed more plausible. An acid transformation associated with the production of gases seemed to cover both fermentation and digestion, as far as the latter was known from the post-prandial ejecta both of man and his intimate, the dog.

Borborygmi and eructations and a sour vomitus seemed to prove that the sometimes stormy processes of our subdiaphragmatic kitchen are closely akin to fermentation, and judging by the charnel-house which tens of thousands of people, quite certainly then as now, carried around in their mouths to poison the body, the notion of putrefaction does not seem so preposterous.

Van Helmont (1577-1644), emerging from the mists of the middle ages, was a believer in the archæus as well as in a special spirit resident in the solar plexus which presided over digestion; with this mystic bed-fellow he associated some definite scientific ideas and insisted on the presence of an acid.

Thus we have as a heritage of the conjectural age of medicine, trituration and attrition, and coction, and putrefaction, and fermentation, and maceration (Haller), and emerging last of all, chemical solution, to be spoken of shortly.

But while men mused on these things during 300 years, a series of fundamental discoveries were being made in the anatomy of the digestive organs, laying bare the fact that a whole series of ducts and absorbents clustered for some puzzling but surely definite purposes around the mouth and the upper intestinal tract, suggesting insistently to the newly arrived scientific mind some positive relation between their activities and the processes of digestion, and raising questions bound to be answered in time, however entangled at first in a maze of conjecture and crude theories.[2] Chief among these discoveries in order of time were the lacteals by Aselli (1622), the pancreatic duct by Wirsung (1642), the thoracic duct and the *receptaculum chyli* by Pacquet (1651), the intestinal lymphatics and their connection with the thoracic duct (1656), and the parotid duct by Steno (1662).[3]

How well might the fortunate scientists in that golden era have applied to themselves the proverb, "It never rains but it pours."

We may fittingly close the hazy epoch of undisciplined guesses, philosophical contemplation, and ignorance with William Hunter's caustic comment on the school of lucubrationists and ratiocinationists: "Some physiologists will have it that the stomach is a mill, others that it is a fermenting vat; others, again, that it is a stew-pan; but in my view of the matter, it is neither a mill, a fermenting vat nor a stew-pan, but a stomach, gentlemen, a stomach."

Lafayette B. Mendel in a charming tribute to John R. Young,[4] divides the history of the effort to understand the physiology of digestion into three eras. The first may be said to end (and, I think, this is the consensus of all physiologists), with Haller's "Elementa Physiologiæ," published in 1757. Not that Haller discovered any fact relating to digestion, for his own idea was that of a simple *process of solution*, but because he rendered the necessary service of gathering between two boards the various conflicting views for comparison, and because he stood on the threshold of the modern chemical era, when the pregnant clouds were gathering over the thirsty land ready to pour down their refreshing discoveries over a period destined to stretch through the next century and a half.

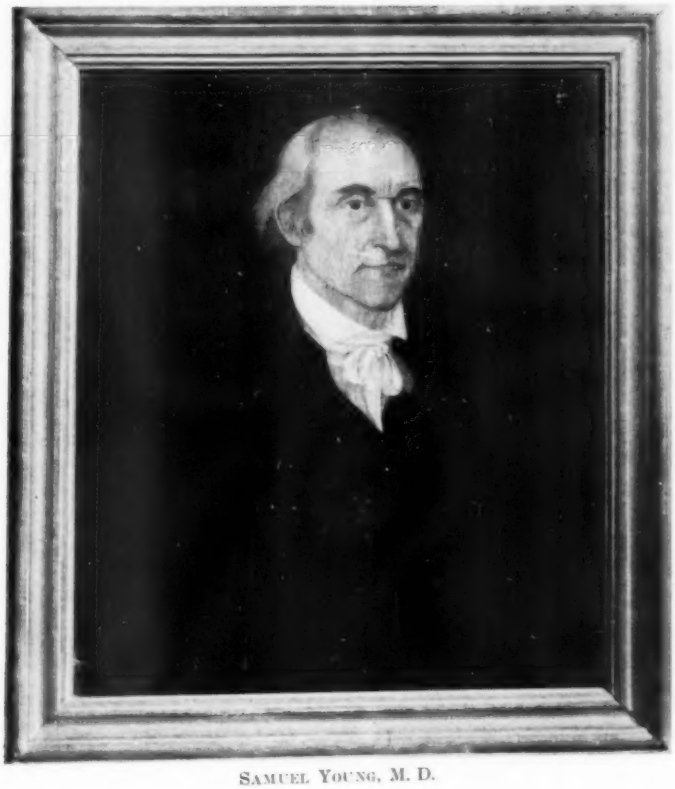
Commencing with the Haller date, and indeed a little before it, we therefore enter the modern experimental or second era, which is illuminated at the very outset by such names as Réaumur (1683-1757) and Spallanzani (1729-1799), and these two, indeed, ought to be hyphenated, for together, as we

[1] Read before The Johns Hopkins Hospital Historical Club, April 8, 1918.

[2] For further data see an admirable résumé by R. J. Cary, in the Bulletin of The Johns Hopkins Hospital, May, 1916.

[3] Garrison: Hist. of Med., 2d. ed., 1917, pp. 237 and 238.

[4] Popular Science Monthly, February, 1909.



SAMUEL YOUNG, M. D.

JOHN R. YOUNG, M. D.

REVERSE OF MINIATURE.

Mr President
and
Gentlemen,

When we take a view of animated Nature, we find that all are subject to a decay- now is man an exception from this, the continual evacuations from different parts of his body are sufficient proofs of this general proposition- As a waste is therefore continually going on in his body it becomes a principle, absolutely necessary to his life that he have means to counteract this general loss of his system- these are the taking in of food and converting it into a nutritious fluid, so that it may be distributed to the several parts of the body, to repair this general loss- Nor is Nature here wanting in her accustomed beneficence, least she should, this food she has connected the want of it with that strong and insufferable, craving, called hunger, and the gratifying this hunger to be accompanied with pleasure.

GRAVE OF JOHN R. YOUNG, HAGERSTOWN.

view them in the perspective of a hundred and fifty years, they blazed a path into the unknown which every investigator has of necessity followed from that day to this.

Mendel's third stadium covers the period of the chemistry of digestion. Hence it is naturally coincident with the rise of modern chemistry, and may be said to begin with the year 1800, and, I would claim, with the work of our hero, John R. Young, of Maryland. More precisely, this era blazoned out with the discovery of free hydrochloric acid in the gastric juice in 1824 by Prout (1785-1850), right after which came the great American work of William Beaumont in 1833, who, living from 1785 to 1853, experimented upon Alexis St. Martin, "the man with the lid on his stomach" through which the processes and the steps of digestion were conveniently investigated in some 238 experiments.

In order to advance more specifically my claims for John R. Young, I must at least epitomize the work of Réaumur and Spallanzani just mentioned. Cary calls the year 1752 a "red-letter year" in the history of digestion, as it was in that year that Réaumur published two treatises on the "Digestion of Birds," the first dealing with the digestion of grain-eating birds with a gizzard, a stout, muscular stomach. Food was put in metal tubes open at the ends, except for a wire grating, which kept the food but did not exclude the gastric fluids; as the food remained unchanged he concluded that the gizzard contained no solvent fluid capable of digesting the aliment. His second memoir dealt with carnivorous birds having a membranous stomach. Here he found that digestion was effected by a gastric fluid, some of which he secured by putting sponges in his tubes; when these were ejected he squeezed out an opalescent, salty, rather sour fluid, which used as an artificial digestant resisted putrefaction.

Spallanzani reviewed Réaumur's work, confirmed his findings, and greatly enlarged its scope. His way of experimenting was to introduce perforated tubes into the stomach, fastened with a wire around the neck of the animal, so that he could conveniently pull the tube out from time to time as he noted the steps of digestion. While testing a great variety of aliments in tubes, he, also, himself swallowed thin linen bags containing food, which he secured for investigation after their passage *per anum*. He also obtained gastric liquor by forcing himself to vomit before breakfast.

"We owe thus to Spallanzani," says Cary, "after Réaumur, the definite experimental proof of the solvent power of the gastric juice upon the various constituents of food, but he was unable to go much beyond this, because he failed to recognize its acid character. He, however, conclusively disproved the older theories of digestion, especially that of trituration, putrefaction, fermentation and maceration." Spallanzani's theory was that of a chemical solution.

The first English experimenter on these fruitful lines appears to have been Stevens of Edinburgh, who, in 1777, wrote a dissertation entitled "De Alimentorum Concoctione."

Great and fundamental as was the value of the observations of Réaumur and Spallanzani, still greater was the fact that they established the absolute necessity of experimental methods in investigating digestive processes. In doing this they lighted a torch never to be extinguished.

In striking contrast, and so forming a happy setting to his pupil's work, is the thesis of Benjamin Rush, Young's pre-eminent teacher in medicine, which by a happy coincidence had been devoted to identically the same topic 35 years before, and offered for his doctorate in the University of Edinburgh. Its title is *"Dissertatio Physica Inauguralis De Coctione Ciborum in Ventriculo."* Rush, too, selected an illuminating motto from Verulam (Bacon), *"Omnino Scientia ex naturae lumine petenda, non ex antiquitatis obscuritate. Nec refert quid factum fuerit; illud videndum quid fieri possit."* The first full-page dedication is to Benjamin Franklin, ambassador to Britain.

Rush begins his dissertation as to the nature and functions of the gastric juice (*"succus gastricus"*), by complaining, *"Dolendum est liquorem gastricum in ventriculo adeo sepultum esse, ut experimentis nostris subjici recuset."* Réaumur's work was clearly not known to him.

Rush then goes on to state that, as far as conjecture can decide, this *succus* is a thin fluid almost of the same nature as saliva, and that it acts vicariously with the saliva. Pigs, for example, which have little saliva, have an abundance of gastric juice. Rush discusses the question of an acid ferment, suggested by van Helmont, and disposes of it, stating that his experiment (given at the end) proves that it is not necessary that an acid ferment should ever be present in the stomach. He and his friend, William Penny, were wont, with commendable zeal, to throw up their meals for test purposes. Rush uses these words, concluding that the "coctio" of the food in the stomach is a process of fermentation *"Spectanda nunc sunt phaenomena coctionis in ventriculo, quae consentire phaenomenis fermentationis miro modo videntur. In omni mole ferente observantur inflatio, extricatio aeris, et mutatio integra molis ferventis. Sed haec omnia nobis coctio ciborum in ventriculo exhibet."* Rush ends with thanks to his master, William Cullen, who suggested his subject, addressing him, *"Vale egregium academiae decus."*

Coctio clearly means the act of digestion in whatever way effected, and is a generic and not a specific term.

Benjamin Rush was easily the master mind in medicine in his day, and his title to be called the modern Hippocrates, and the American Sydenham, was hardly then disputed; but I venture to suggest that he appears in this thesis, as in the work he was destined to do through his following maturer decades, rather as the highest expression of the wisdom already attained than as a pathfinder; he had no genius, no premonitions, and flashed no light into the future.

How little did Rush realize that in that class of 1803 there sat on the benches a country boy from Western Maryland who had a certain rare quality, lacking in himself and in his eminent colleagues, an imagination and a spirit of investigation and persistence, tempered by sound judgment, for which the world is ever waiting; a spark of the same fire which burned in the breast of Vesalius, and of Harvey, and in Réaumur and Spallanzani. Rush had his unquestioned merits,

and holds his accredited place in the evolution of medicine in our country, but Young's name will shine with an ever brighter luster, as the one who first effectively introduced and patiently followed out in this country the modern laboratory methods. Young was our first real scientist in the field of medicine, and was the first to take the fundamental step of demonstrating that the gastric juice is an acid, with solvent, anti-putrefactive properties. Van Helmont had noted the acid long before but it had been forgotten; John Hunter had stated it and had then qualified his statement until it had no force; Young made it the subject of his thesis, demonstrating his contention by numerous experiments, and so took this first essential step forward in the study of the chemistry of the digestion.

Young showed that the gastric juice had its origin in a gastric secretion, and that it did not arise from any kind of a fermentative process, vinous, acetous or otherwise. He also noted the important fact that the flow of the gastric juice and that of the saliva were synchronous.

Young's thesis was, therefore, notable and marks a distinct advance in the physiology of digestion. He first takes a stand against the teaching of Cullen, all-powerful in his day, who held that food received into the stomach underwent fermentation with the formation of an acid. Young declares, "That an acetous fermentation takes place in the human stomach in a healthy state, we entirely reject."

Young was peculiarly favored by our North American fauna, for he made his experiments on our big bull-frog, then called *rana ocellata,* whose large esophagus enabled him to insert a *rana pipiens* into its stomach with a thread tied to its leg. He pulled the small frog out at intervals and noted the steps and rapidity of digestion and, disputing the theory of putrefaction, remarked that there was no odor of decomposition.

He introduced a calculus into the frog's stomach and found it gradually dissolved, and recommended this method of treating calculi in the human bladder (as others had done before him) by ladling juice out of a frog's stomach with a teaspoon and putting it into the bladder. He put beans, peas, wheat and bread into the frog's stomach and found that in 30 hours the beans, peas, and wheat were not in the least acted upon, but that the bread bag was empty; but when the cereals were crushed he found that they were digested.

He then deals at greater length with the question of fermentation in the stomach, and investigates the three kinds, "vinous, acetous, and putrefactive." An accommodating friend took a meal of sugar and regurgitated it several hours afterwards, when no vinous fermentation was found.

Young himself dined on "chicken pye," and irritated the fauces so as to eject the "pye"; here also he found no acetous change after further warming the ejecta for nine hours. That the acid in the stomach does not come from fermentation, he proved by putting litmus in the stomach of the frog, as well as by removing and examining the food before any fermentative process could have taken place.

Of the experiment on himself, Young says: "I took some meat on an empty stomach: in half an hour afterwards, by irritating my fauces, the meat was thrown up, and with it some gastric fluid: upon being tested, an acid was very evidently present. Here no one can suppose the acid was to be referred to the meat. We have little hesitation, therefore, in saying that the acid so constantly found in the stomach of man and, probably, almost all animals, is to be referred to their gastric fluid. Having thus, we hope, traced the acid of the stomach to its proper origin, we next attempted to ascertain its nature by chemical tests. Mr. Mitchell being in good health, and having the power to ruminate, frequently threw up the contents of his stomach for me; which being filtered, a transparent and acid fluid was obtained, on which the following experiment was performed: To a portion of this fluid, acetate of lead was added, a white precipitation immediately took place; this being washed, muriatic acid was added, which decomposed it, a very white powder remaining at the bottom, and a fluid above, etc." His conclusion was that he was dealing with phosphoric acid. What a pity that he did not recognize the fact that the very acid he held in his hand, as he added it to the fluid was the acid he sought, thus placing another great discovery to his credit!

In the course of these experiments Young emptied the stomachs of snakes, as well as of frogs, after feeding them on various materials—flesh, bones, teeth, vegetables and cereals.

He explains the process of digestion as follows: "We would therefore explain this process in a few words. Aliment is dissolved by the gastric menstruum; it then passes into the duodenum and meets with bile and pancreatic liquor; after being united with these, a heterogeneous mass is formed called chyme, and from this the lacteals secrete chyle."

He concluded that the tissues absorbing the chyme must play a vital part in the process, and not merely act as absorbents, because the fluid found in the lacteal vessels was always the same to taste, whatever might be the character of the food partaken. He notes in this connection that a patient of Dr. Wistar's lived for many weeks on rectal enemata alone, where bile and gastric juice and pancreatic liquors could not have assisted in the process of absorption.

Mendel adds this comment: "One hundred years later the obscure importance of the absorbing alimentary tract must still be emphasized. In the words of a popular text-book, the energy that controls absorption resides in the wall of the intestine, presumably in the epithelial cells and constitutes a special form of imbibition which is not yet understood. Thus the dignity of the living structures still remains unchallenged."

Young's work was done in a simple, unpretentious effort to discover the secrets of nature by going direct into her house and asking questions. He disposed of the excogitated imaginary hypotheses of his predecessors and left his subject on the simple basis of established fact. He was the first in this country to take the necessary steps in an entirely new direction, leaving it to his followers to advance step by step, following no other general methods than those used by himself. He was both a pathfinder and a sign-post; he cried out, "Come, stand here; this is the solid ground," and he pointed out the direction to subsequent progress.

Young was the very first American medical man to enter the new field of fruitful experimentation, and to bring home his own sheaf for the garner. With prophetic foresight he takes his motto for the title-page of his thesis from the great Frenchman, the father of modern chemistry, himself an experimenter in physiology, Lavoisier, who declared: "We ought in every instance to submit our reasoning to the test of experiment and never to search for truth but by the natural road of experiment and observation." It was the new spirit of a new age which we of English stock like to trace to Bacon, who laid down the maxim, cited by Professor Mendel, "*Non fingendum aut excogitandum, sed quid natura faciat observandum,*" which I venture to render after a liberal fashion.

Long and weary is the way of ratiocination.
Nothing fruitful ever comes from tedious lucubration.
Nature's ways are only found by patient observation.

WHAT YOUNG DID FOR DIGESTION

(1) He did away with the theories of innate heat and vital spirits as the essential factors in the act.

(2) He did away with the notion that digestion was essentially a process of trituration, fermentation, or putrefaction.

(3) He showed that it was effected by an acid which he attempted to analyze, and concluded that it was phosphoric acid.

(4) He experimented on animals and on men (himself and a friend).

(5) He secured pure gastric juice and experimented with it *in vitro*.

(6) He showed that the acid gastric juice checked putrefaction.

(7) He drew the inference that dyspeptics ought not to dilute the gastric juice with water.

Young has been a most mysterious figure in American medicine, and until now nothing has been known about him, aside from the fact that he went from Hagerstown to the University of Pennsylvania, where he studied medicine, and that he wrote a remarkable thesis; after which he disappeared from sight as completely as if the earth had swallowed him. Even the significance of the middle letter of his name has not been known.

Let me present categorically the hitherto known facts: (1) His valuable thesis on digestion; (2) his name, known in part; (3) the place of his birth (his own town has completely forgotten him); (4) the year of his graduation, after which he disappeared into oblivion.

I now give the results of some investigations I have been making for the past year.

John Richardson Young (let me announce his full name given for the first time in public since his death 114 years ago) was born in Hagerstown, then called Elizabeth-Town. He was the son of Samuel and Ann Richardson Young. His mother died in 1791, at the age of 31, when her son was nine years old, and at his death, thirteen years later, he was laid beside her in the old St. John's burying-ground on Mulberry Street at Hagerstown.

The father, Dr. Samuel Young, was a native of Ireland, a graduate of Trinity College, Dublin, and received his medical education in Edinburgh; he came to this country before the Revolution, and "attained a high position as a physician and a good man."

John Richardson Young was graduated from Princeton University (then the College of New Jersey) in 1799, when he was seventeen and, while there, was a member of the Cliosophic Literary Society.

The study of medicine was begun with his father, from whom he received, as he says in the dedication to his graduation thesis, his "first principles of medicine." The affectionate relation between father and son is shown in other instances, an intimate one being the purchase of a watch made in London in 1804, and given to his son the same year, the year after his graduation, several months after he had joined in practice with his father, and the year of his death.[5]

John R. Young continued his medical education at the University of Pennsylvania, arriving in Philadelphia "Sunday 7th of November, 1802," as a small note-book records in his own hand-writing. He graduated on June 9, 1803, with the thesis which is his title to fame.

Instructors in the medical part of the University while John R. Young was a student were: Dr. William Shippen, anatomy, surgery, midwifery, with Dr. Caspar Wistar, adjunct; Dr. Benjamin Rush, institutes of medicine and clinical medicine; Dr. James Woodhouse, chemistry; Dr. Benjamin Smith Barton, materia medica, botany, and natural history. Dr. Rush at this time was attending also to the duties of the chair of theory and practice of medicine, made vacant by the death of Dr. Adam Kuhn, to which chair Rush was regularly appointed in 1805.

John Andrews, D.D., provost *pro tem.* at the time of Young's graduation, was also a Marylander, born in Cecil County in 1746; he was ordained a clergyman in the Church of England in 1767 in London, England, was a missionary at Lewes, Delaware, and received his degree of Doctor of Divinity from the newly-established Washington College in Maryland in 1785. He was headmaster of the Academy of the Protestant Episcopal Church of Philadelphia from 1785-1789, and in this latter year was made professor of moral philosophy in the restored College of Philadelphia. In his provostship he succeeded Dr. McDowell from 1810 to 1813.

There were 15 members of Young's class, one of whom, John Stevenson Mitchell, of Pennsylvania, was probably the "Mr. Mitchell" who lent himself so obligingly to Young's experiments.

While a student at the University of Pennsylvania, Young fell under the special notice of Dr. Benjamin Smith Barton,

[5] **This watch is now owned by Mr. T. Elliott Patterson of Philadelphia, who carries it, and who tells me that it keeps correct time. Mr. Patterson, who was present at the reading of the Young paper before The Johns Hopkins Hospital Historical Club, exhibited the watch.**

who became his friend as he was his teacher; to him, also, Young dedicates his thesis.

Young's thesis was published by Eaken and Mecum, Philadelphia, 1803. This edition is rare; a copy is in the Library of the Surgeon-General at Washington, and the copy which belonged to Benjamin Rush is in the Ridgway Branch of the Philadelphia Library.

The work is contained, also, in Caldwell's "Medical Theses," 1805, which can be seen at the library of the Surgeon-General. There is also a copy in the Medical and Chirurgical Library, Baltimore.

John R. Young found his professional billet awaiting him on graduating in June, as is evident from an advertisement July 13, 1803, in the *Maryland Herald* and *Elizabeth-Town Weekly Advertizer*.

NOTICE

Having taken my son, Doctor John R. Young, as a partner in the practice of physic; all those indebted to me are therefore requested to settle up their accounts to this date, July 13, 1803.

(Signed) Samuel Young.

John R. Young was one of the first contributors to Barton's *Philadelphia Medical and Physical Journal*, and his article, appearing in the first volume, on a "Case of Tetanus Cured by Mercury," bears the date March 29, 1804, but the publication did not appear until the autumn, several months after Young's death, and Barton in a footnote says, "Some account of this truly ingenious and amiable young man will be given in a future number of this Journal." This sketch, however, never appeared.

In the same volume of the *Journal* (p. 145) is an extract from a letter by Young recording his use of "Saccharum Saturni in cases of uterine hæmorrhage with complete success." This letter has the same date, March 29, 1804.

An unpublished manuscript written by Young has been found among his effects and forms an interesting addition to his writings. The paper is a clear, simply-worded exposition of digestion, evidently prepared to be read before a mixed audience and before his own work in that subject had been broached. The manuscript is neatly written and bears corrections in several places in another hand, probably that of his father, Dr. Samuel Young.

Young was one of the founders of the American Linnean Society, of which Benjamin Smith Barton was president, and was a member of the Philadelphia Medical Society.

There is one more brief, sad item to be added about this earnest young physician: it is to be found in *The Maryland Herald* and *Hagers-Town Weekly Advertizer* of June 13, 1804, just 11 months later than the former notice: "Departed this transitory life on the 8th instant in the 22d year of his age, John R. Young, M. D., of this Town, after a long and tedious illness." Following this are two poems laudatory of the virtues of the departed; one is signed "Corydon," and the other "Erigena."

On a beautiful spring day, recently, I visited the grave of John Richardson Young in the old St. John's churchyard. A fine slab of sandstone marks his resting-place, inscribed with this legend:

In Memory
of
John R. Young M. D.
Who Departed This Life
on the 8th Day of June 1804
in the 22d Year of His Age
"Nec prosunt domino quae prosunt omnibus artes"

Pause stranger on this sacred spot
Here give to worth a parting sigh
So may thy grave be ne'er forgot
When the lorn stranger passes by.

The grave of the father is separated from that of his son by the graves of two sisters of John R. Young, who died at the ages of 21 and 30, respectively. He lived 34 years after the death of his gifted son, and was 108 years old when he died in 1838, as attested by his gravestone.

From Hagerstown I journeyed across the mountains to the little town of McConnellsburg, which is near "Brookside," the old homestead of the Pattersons, beautifully situated in a mountainous basin in Fulton County, the wildest part of Southern Pennsylvania. Here live Miss Bessie Bell Patterson and her two brothers, William Calvin and John Lind Patterson, whose mother, Mrs. Isabella Milligan Patterson, was the second cousin of our John R. Young.

In this attractive mountain home I saw an exquisite miniature of John R. Young, painted on ivory by Peale, and an oil portrait of old Dr. Samuel Young.

The portrait of John R. Young shows a youth in early manhood with an oval face, curling brown hair coming down over the forehead, blue serious eyes, dark, finely-marked brows; neither mustache nor beard is worn; the face reveals both character and intellect. The reverse of the miniature bears two gold bands with rich blue glass between, and in the center is woven the chestnut hair of John R. Young, with the delicately wrought intertwined gold initials J. R. Y.

Old Dr. Samuel Young's life-size bust, at the age of 74, shows him tall and slim, with sloping shoulders. The face is that of an old man with scant gray hair, blue eyes, thin lips, compressed, determined mouth, and fine intellectual face. The portrait was painted by J. Frymier, three months after the son's death.

There is a family tradition that John R. Young as well as his two sisters died of tuberculosis. Dr. H. B. Jacobs suggests that the mother, dying at the early age of 31, may have had the same disease and have transmitted it to her children.

I have ventured to draw at some length on the various memoranda which have grouped themselves about the name of John R. Young, as but a just tribute to a young man of great promise in the early history of American medicine. After the lapse of 114 years we can well afford to honor his memory not only for his great achievement, but as an expression of thankfulness for the spirit which animated him—that rare spirit which alone has been the beacon light of our profession as it has groped its way out of Cimmerian darkness into the light of to-day.

He first caught the lighted torch, flashed it out into the darkness and passed it on to Beaumont, who sent it on down from hand to hand, through the century, renewed and nourished by each zealous hand that grasped it until its brilliant, steady glow illuminates the whole land.

In the preparation of this paper personal communications have been received from Miss Bessie Bell Patterson; Mr. T. Elliott Patterson; Dr. Ewing Jordan; Judge T. J. C. Williams; Dr. John McPherson Scott; Miss Mary L. Titcomb, librarian, Washington County Public Library; Mrs. O. H. W. Hunter, Hagerstown.

To Dr. Jordan I am particularly indebted for supplying the middle name of John R. Young, and for putting me in touch with the living members of the Young family.

The Presbyterian Church Records (by the courtesy of the Rev. J. Russell Garr) and the Court-House Records (by the courtesy of Mr. Thomas E. Hilliard, register of wills, and Mr. Edward Oswald, clerk of the court of Hagerstown) were consulted; and the following books besides those named in the bibliography: Catalogue University of Pennsylvania with an Historical Sketch, 1836; Scharf's History of Western Maryland; Williams' History of Washington County; Cordell's Medical Annals of Maryland.

Some of the most valuable data I have been able to secure have come into my hands through the indefatigable labors of Miss Harriet Blogg, who has followed with profit some exceedingly exiguous clues, and who has in addition visited Hagerstown, held numerous interviews, and has inspected and secured a copy of the will of old Dr. Samuel Young.

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THE BLOOD PRESSURE IN AMYLOID DISEASE OF THE KIDNEY

By K. HIROSE

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Since the time of Rokitansky so many have studied the influence of amyloid disease of the kidney upon the blood tension that it might appear that little remained to be done. Nevertheless, at the suggestion of Dr. Welch, the following attempt has been made to ascertain, (1) whether amyloid ever occurs in the kidney without nephritis, (2) what types of nephritis are associated with amyloid, and (3) what changes in the blood pressure and in the condition of the heart and arteries accompany amyloid disease of the kidney.

HISTORICAL SURVEY

Rokitansky was the first to recognize amyloid disease of the kidney (1842) and distinguished it under the name *Speckniere* from other forms of Bright's disease. Virchow, who studied the chemical peculiarities of the amyloid substance, also separated as belonging to a third form of Bright's disease those cases in which the kidneys contained amyloid. Weigert tried to differentiate several forms of amyloid disease and found that, although there are a few cases in which the amyloid exists in the arteries without other change, there is generally a profound modification of the kidney substance. The most common form is the so-called large white kidney. Bartels also noted the frequent association of amyloid with chronic parenchymatous nephritis, although he found it only rarely with contracted kidneys. Cornil and Ranvier state that there is always an associated parenchymatous nephritis. Wagner divides amyloid disease of the kidney into four forms characterized by the presence of: (1) Slight amyloid of the cortex and medulla without change in the epithelium or stroma, (2) slight amyloid with fatty degeneration of the epithelium but with normal stroma, (3) amyloid with fresh interstitial changes in the kidney, and (4) the amyloid contracted kidney. Grainger Stewart divides Bright's disease into three forms, of which one is the amyloid form, and recognizes periods in its development: (1) The period in which there are practically no macroscopic changes, (2) the period of swelling, and (3) the period of contraction which may become extreme.

Charcot, Rosenstein, Leyden, Aufrecht, Litten and Raubitschek express essentially similar views.

As to the condition of the heart and the state of the blood pressure in amyloid disease of the kidney, the opinions of writers upon this subject are almost in agreement.

Weigert and Bartels find no enlargement of the heart and no increase in blood pressure, while Wagner and Rosenstein state that hypertrophy of the left ventricle may appear rarely in as-

sociation with amyloid kidneys and then only when there is an advanced contraction of the kidney. Raubitschek found no hypertrophy of the ventricle in cases of pure amyloid disease of the kidney and T. C. Janeway agrees with this view. Geisböck, Buttermann, Hensen, Hayaski and others report cases of amyloid disease involving the kidneys, with subnormal blood pressure.

It is evident from the foregoing that while the presence of amyloid in the kidneys is associated with various forms of nephritis, the impression prevails that there is no hypertrophy of the heart and no increase of blood pressure.

Material

Of 87 cases of amyloid disease collected in the pathological departments of The Johns Hopkins University and Bay View hospitals, 59 were selected which showed definite amyloid changes in the kidneys. Sections were stained by the various well-known methods and the cases analyzed and tabulated to show the condition of the kidneys, heart and other organs as well as the state of the blood pressure and other clinical conditions. These tables are, however, so extensive as to make their publication impossible, and we have been content with a summary of the results of the analysis.

Pathological Anatomy

The changes in the kidneys are extremely variable. Amyloid is found in the glomeruli, in the other blood vessels of the kidney and in the walls of the tubules.

The glomeruli were practically always involved. There was one case, however, showing amyloid in the spleen, liver and other arteries of the kidney in which the glomeruli were free. Such cases have been reported by many authors (Schmitz, Rosenstein, Kyber, Litten, *et al.*), while Kyber also reports one in which amyloid was found in the glomeruli only.

The remaining blood vessels were affected in all but 13 cases, while the walls of the tubules showed amyloid less often. There is marked variation in the quantity of amyloid deposited in the various parts of the blood vessels, a fact which has long since been recognized.

The epithelium of the tubules showed changes in practically all the cases, appearing almost normal in only one instance, in which, however, there were rather extensive scars. In general, the tubules were dilated with swollen granules or fatty epithelium or were lined with much-flattened cells. Granular and hyaline casts and epithelial debris were common.

The interstitial tissue was increased in amount and infiltrated with wandering cells in all but 10 cases which showed no changes. In 22 cases the stroma was especially increased, diffusely in some cases, but in others particularly in the cortex round the glomeruli.

It is evident from this that in every case there was at least a trace of nephritis with degenerative changes in the epithelium of the tubules and scarring of the most affected areas.

The question arises as to the relation between the amyloid deposit and the other changes in the kidneys, and it is most important to know if possible whether both were caused by the same etiological factor or whether the formation of amyloid preceded and caused the nephritis, or the nephritis the amyloid.

That the succession of events is not the same in all cases is clear from the following facts. In the amyloid kidney there is sometimes extreme fatty degeneration of the epithelium with very slight amyloid change or, on the contrary, extreme amyloid change with very slight alteration of the parenchyma of the kidney. Indeed there are cases in which, in the presence of amyloid changes in spleen and liver, the kidneys show parenchymatous changes only.

On the whole, there seems to be little reason to believe that the amyloid itself can play any part in causing the nephritis. Rather it is possible that the disease which causes the production of the amyloid is also capable of producing changes in the kidney substance. Nevertheless, the fact that one may find kidneys in an advanced stage of contraction and scarring in which amyloid is beginning to appear seems to show that the amyloid may be developed secondarily.

Blood Pressure

It is generally stated that in contrast with the cases of nephritis uncomplicated by amyloid, the blood pressure in cases of nephritis with amyloid is not increased. This appears to be supported in this series, although there are six cases in which the heart weighed over 400 grams. Unfortunately the blood pressure was not exactly measured in these, but is merely noted as "good tension" or "fair tension," except in one case, in which the heart weighed 440 grams and in which the systolic pressure was 120 mm. In 13 other cases in which the measurements of the pressure were made the heart did not exceed 300 grams in weight and was generally below 250 grams. In these the systolic pressure ranged from 90 to 120 mm. Hg. and the diastolic from 60 to 90 mm.

It might be thought that the cases in which the heart was enlarged were especially those in which the development of a chronic nephritis with contracted kidney had preceded the appearance of amyloid and therefore a survey of the weight of the kidneys might be of interest. In 40 cases the kidneys weighed more than 300 grams; while in nine only did they fall below this weight. In the cases in which the heart weighed over 400 grams, the kidneys weighed 400, 500, 550 and 300 grams. There were two other cases in which there were small granular kidneys. Thus the great majority of the kidneys in which amyloid is found are distinctly larger than normal, and even in those cases in which the heart is enlarged there were only two cases in which the kidneys had the character of contracted kidneys. Of the 11 cases in which the combined weight of the kidneys was below 300 grams, only one presented a heart of weight greater than 350 grams.

The reason for the absence of cardiac hypertrophy and of heightened blood pressure in cases in which there is amyloid disease of the kidney is quite unknown. Geisböck found that

in most cases of tuberculosis the blood pressure is low, and Bouveret emphasizes the fact that hypertrophy of the heart may be lacking in chronic nephritis where there is also senility, tuberculosis or other cause of cachexia. The suggestion that the low blood tension may depend upon a coincident extensive destruction of the adrenal by the deposit of amyloid is not convincing, since it is by no means proven that the high blood pressure in nephritis is brought about by the adrenal secretion. In this series, 12 cases showed involvement of the adrenals, but of these one at least showed a high blood pressure and another a great hypertrophy of the heart.

Œdema appears to be a not uncommon symptom of amyloid disease and was present in 21 of these cases. Rosenstein found it in 61 of 72 cases, Fehr in 98 of 152 cases, while Grainger Stewart found it in only 6 of 100 cases.

From the analysis of the cases it was found that tuberculosis occurred in 28 and syphilis in 22. Other chronic infections were also found, often in connection with these, so that the cause of amyloid disease cannot be regarded as simple.

Thirty-two cases were male and 27 female. Fehr reports 89 cases in males and 63 in females.

With regard to age, it was found that most of the cases died in the third decade, as shown in the following table:

Age	1-10	11-20	21-30	31-40	41-50	51-60	61-70
Dickenson 61 cases.....	3	11	21	10	10	3	3
Fehr 144 cases	6	24	43	36	23	7	7
Hennings 76 cases	3	19	21	20	7	3	2
Rosenstein 32 cases	0	1	11	5	9	4	2
Hirose 59 cases	0	3	18	12	15	8	3

The excess of deaths with amyloid diseases in the third decade is probably due to the fact that tuberculosis is so common in persons of that age.

It is striking that of the 59 cases, 26 were negroes, in spite of the fact that more whites than negroes were treated in the hospital. Lambert thinks that the influence of race upon the incidence of amyloid is negligible. In oriental countries, especially in Japan, it has been thought rare, but recently Japanese authors (Katsurada, Miura, Matsuo, Nagayo, Sugai, Tanaka, Tsunoda, Takesaki, Yamagiwa) have reported many cases in which amyloid disease was advanced.

SUMMARY

1. In a series of 59 cases the presence of amyloid in the kidneys has always been associated with chronic nephritis. It is impossible to determine whether the nephritis antedated the amyloid or was developed coincidentally with it. In 40 cases in which measurements were given the kidneys were larger than normal, while in nine they were small and granular.

2. In all but one of the 15 cases in which the blood pressure was recorded it was found to be normal or below normal. In the one case in which the systolic pressure was 170 mm., the kidneys were rather large and there was no cardiac hypertrophy.

3. Of the 59 cases, 10 showed cardiac hypertrophy, but only one of these was associated with small granular kidneys, and in none was high arterial tension noted.

It appears from this that even if it be assumed that a persistent nephritis produced cardiac hypertrophy and hypertension, the advent of the amyloid-forming process must have reduced the blood pressure to a low point and may even have caused a retrogression in the size of the heart.

In conclusion, it gives me great pleasure to extend here my heartfelt thanks to Professors Doctors Welch and Winternitz, and to express my sincere appreciation of their keen interest in this study and of their many helpful suggestions and directions. Moreover, I beg to acknowledge my obligation to the physicians in The Johns Hopkins Hospital and Bay View Hospital who have kindly permitted me to publish the clinical histories.

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